IN THE UNITED STATES PATENT & TRDEMARK OFFICE

In re Patent Application of:

Mitchell E. Reff, et al.

Application No. 09/292,053

Filed: April 14, 1998

For: GAMMA-1 ANTI-HUMAN CD23 MONOCLONAL ANTIBODIES AND USE THEREOF AS THERAPEUTICS

Group Art Unit: 1644

Examiner: M. DiBrino

DECLARATION PURSUANT TO 37 CFR §1.132
BY RICHARD G. LIZAMBRI, M.D.

I, Richard G. Lizambri, M.D., declare as follows:

1. I am, and have been for the past three years the Director of Autoimmune and Inflammatory Diseases at IDEC Pharmaceuticals Corporation. My qualifications in the field of autoimmune disease are further summarized in my attached Curriculum Vitae.

2. I am familiar with the above-identified United States patent application and the technology disclosed and claimed therein. I have also read the Office Action mailed June 4, 2001, in which the Examiner asserts that the use of anti-CD23 antibodies, as claimed, to treat or prevent autoimmune or inflammatory disorders is allegedly non-enabled. I disagree with these assertions as further detailed below.

3. CD23 is a membrane-bound glycoprotein that binds IgE. Membrane-bound CD23 is proteolytically cleaved to yield several soluble forms (collectively sCD23). It is well accepted in the field that CD23 is also implicated in the regulation of IgE synthesis

and IgE-dependent antigen presentation. In addition, it is well accepted that soluble CD23 (sCD23) effects inflammatory pathways in vitro by activating monocytes. Accordingly, it is not only likely but expected that, as claimed, a human disease wherein inhibition of IgE is thereapeutically or prophylactically beneficial can be prevented or treated by administration of an effective amount of an anti-human CD23 monoclonal antibody that inhibits IgE expression.

4. I have supervised a Phase I clinical study of IDEC-152 (an anti-CD23 antibody[1])("Clinical Study") in the treatment of patients with mild persistent or moderate persistent allergic asthma. The results of this Clinical Study confirm that the administration of IDEC-152 resulted in sustained and dose-dependent pharmacologic activity in all dose groups (i.e., 0.05, 0.25, 1.0, 4.0, 10.0, or 15.0 mg/kg of IDEC-152) based on decreases in mean IgE concentrations. (See, Appendix A summarizing this data). Accordingly, as stated above, it is quite reasonable to expect that administration of an effective amount of an anti-human CD23 monoclonal antibody that inhibits IgE expression will be effective in both the treatment and prevention of a human disease wherein inhibition of IgE is thereapeutically or prophylactically beneficial.

5. Not only is anti-CD23 expected to be successfully employed as claimed, it is also expected to be well tolerated by humans. For example, in the clinical trial discussed above no patient treated with IDEC-152 (antiCD23) developed an anti-IDEC-152 antibody titer. Thus, the administration of anti-CD23 antibodies gives every indication of being safe for the treatment and prevention of a human disease wherein inhibition of IgE is thereapeutically or prophylactically beneficial.

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[1] Specifically, IDEC-152 is a PRIMATIZED IgG1 kappa anti-CD23 monoclonal antibody. CD23 is a type II membrane glycoprotein that binds IgE.

6. I am further aware of the depleting activity of antibodies according to the invention. I believe that these properties may be instrumental in the enhanced IgE inhibiting properties of gamma-1 anti-human CD23 antibodies according to the invention. Particularly, the inventive antibodies may result in some B cell depletion, and consequently reduce antibody production versus anti-human CD23 antibodies possessing a different (non-gamma 1) or no Fc constant region.

7. I hereby declare that all statements made herein of my knowledge are true and all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statement and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of the Title 18 of the United States Code and that such willful false statement may jeopardize the validity of the application or any patents issued from them.

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Date Signature